II. REMARKS

Formal Matters

Claims 1, 3, 5, 6, 13-15, 17-21, 33, 35, 36, and 38-43 are pending after entry of the amendments set forth herein.

Claims 1, 3, 5-8, 13-21, and 31-43 were examined and were rejected. Claims 9-12 and 22-30 were withdrawn from consideration.

Claims 1, 3, 5, 6, 13, 18, 20, 21, and 39-43 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1, 3, 5, 13, 20, and 21 is found in the claims as originally filed, and throughout the specification, in particular at the following locations: claims 1 and 13: Examples; paragraph 0010; paragraph 0037; and paragraph 0075; claims 3 and 5: paragraph 0010; and claims 20 and 21: paragraph 0088. The amendments to claims 6 and 18 are editorial in nature. The amendments to claims 39-43 alter claim dependency. Accordingly, no new matter is added by the amendments to claims 1, 3, 5, 6, 13, 18, 20, 21, and 39-43.

Claims 7-12, 16, 22-32, 34, and 37 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Examiner Interview

The undersigned Applicants' representative thanks Examiner Hama and Examiner Shukla for the courtesy of a telephonic interview which took place on June 21, 2005, and which was attended by Examiners Hama and Shukla, inventor James D. Murray, and Applicants' representative Paula A. Borden.

During the interview, the rejection of claims 1, 3, 5-8, 13-21, and 31-43 under 35 U.S.C.§ 112, first paragraph, was discussed.

Rejections withdrawn

Applicants note with gratitude that the following rejections, raised in the September 2, 2004 Office Action, have been withdrawn: 1) rejection of claims 1, 2, 5, 13, and 14 under 35 U.S.C.§102(b); 2) rejection of claims 1-5, 13-15, 20, and 21 under 35 U.S.C.§102(e); and 3) rejection of claims 1-8, 13-17, 20, and 21 under 35 U.S.C.§103(a).

Rejections under 35 U.S.C.§112, first paragraph

Claims 1, 3, 5-8, 13-21, and 31-43 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking enablement. Claims 1, 3, 5-8, 13-21, and 31-43 were rejected under 35 U.S.C.§112, first paragraph, as allegedly failing to comply with the written description requirement.

Enablement

The Office Action stated that the specification is enabling for: a) a transgenic non-human mammal whose somatic and germ cells comprise a nucleic acid sequence encoding stearoyl-CoA desaturase (SCD) operably linked to a mammary gland-specific promoter, wherein the transgene is expressed in the mammary gland of the mammal, and wherein milk of the mammal contains the SCD transgene; b) a method of harvesting or processing the milk, wherein the milk has higher levels of MUFA than milk obtained from a non-transgenic mammal; and c) a method of producing the non-human mammal, wherein the SCD is microinjected into a single-celled non-human mammalian embryo, and wherein the non-human mammalian embryo is transferred into a non-human mammalian female of the embryo's corresponding species.

The Office Action stated that the specification does not reasonably provide enablement for: 1) any transgenic non-human mammal, comprising a transgene encoding any fatty acid desaturase other than SCD; 2) wherein the transgene comprises a coding sequence for fatty acid desaturase, operably linked to any animal tissue specific promoter other than mammary gland tissue promoter; 3) a method for producing the transgenic non-human animal comprising introducing any desaturase transgene into a somatic cell, forming a genetically modified somatic cell, transferring the genetically modified somatic cell into a single-celled embryo, and transferring the genetically modified embryo into a recipient female; and 4) a method for producing a food product, other than milk, from the transgenic non-human animal. Applicants respectfully traverse the rejection.

Fatty acid desaturase genes

The Office Action stated that the specification does not teach any transgenic non-human mammal comprising a transgene encoding any fatty acid desaturase other than stearoyl CoA desaturase (SCD). Applicants respectfully disagree.

The specification provides ample description for how to make and use a transgenic non-human mammal comprising a desaturase-encoding transgene. The specification provides sources for nucleotide sequences encoding various desaturase proteins, which nucleotide sequences were well known in the art as of the priority date of the instant patent application. Specification, paragraph 0066. The specification provides working examples of transgenic non-human mammals comprising a transgene encoding SCD. Using the ample guidance provided in the specification, together with the knowledge and skill level in the art, those of ordinary skill in the art could make a transgenic non-human mammal comprising a transgene encoding any desaturase.

As of the September 17, 2002 priority date of the instant application, a large number of fatty acid desaturases were known and had been characterized enzymatically; and the nucleotide sequences encoding numerous such fatty acid desaturases were known. The instant specification provides the GenBank accession numbers of several nucleotide sequences encoding various fatty acid desaturases.

In the instant application, Stearoyl CoA desaturase (SCD) was chosen as a model fatty acid desaturase, and SCD transgenic mice and goats were generated and characterized. However, one could readily generate a transgenic non-human mammal, as claimed, where the transgenic non-human mammal includes a transgene encoding any of a variety of fatty acid desaturases. For example, if a fatty acid desaturase-encoding nucleotide sequence were under transcriptional control of a mammary gland-specific promoter, one would reasonably expect that such a transgenic non-human mammal would produce milk having a level of monounsaturated fatty acids (MUFA) that is higher than the level of MUFA in milk of a non-transgenic mammal of the same species. This is because the structures of a wide variety of fatty acid desaturases are known and are conserved.

The Office Action stated that the art teaches that the family of fatty acid desaturases is vast, and that an artisan cannot predict whether any fatty acid desaturase from any species of mammal would necessarily have the same enzymatic activity as it has in the original animal. However, claim 1 recites that a tissue of the transgenic non-human mammal comprises a level of MUFA that is at least 5% higher

than the level of MUFA in the same tissue of a non-transgenic mammal of the same species. The specification provides ample description as to how to measure the level of MUFA in a tissue of a transgenic non-human mammal. All that would be required to determine whether a given fatty acid desaturase transgene, when expressed in a transgenic non-human mammal, resulted in a higher level of MUFA in a tissue of the mammal, would be to measure the level of MUFA in the transgenic mammal. The specification teaches how to accomplish such. Accordingly, the specification is enabling for the full scope of the claims.

The Office Action stated that an artisan cannot predict if any transgene can be expressed in any species of animal. However, the specification teaches how to determine whether a given transgene is expressed. Furthermore, those skilled in the art are well aware of various methods of determining whether a transgene is expressed. Accordingly, the specification is enabling for the full scope of the claims.

The Office Action stated that the specification does not teach the use of a desaturase that catalyzes the formation of double bonds in a fatty acid such that an animal could make PUFAs. The Office Action stated that SCD cannot catalyze the formation of fatty acids with more than one bond, to make PUFAs. However, SCD can in fact catalyze the formation of fatty acids with more than one double bond, to linoleic acid. An example of one type of a polyunsaturated fatty acid that can be generated by SCD is a conjugated linoleic acid (CLA). An example of a CLA that can be generated by the action of SCD is C18:2 cis-9 trans-11 fatty acid. The data presented in the instant application demonstrated that the level of CLA is increased in SCD transgenic goats. See, e.g., Figure 1C.

Tissue-specific promoters

The Office Action stated that the specification does not reasonably provide enablement for a transgenic non-human mammal, where the transgene comprises a coding sequence for any fatty acid desaturase, operably linked to any animal tissue-specific promoter other than mammary gland tissue promoter. Applicants respectfully disagree.

The instant specification provides ample description of various tissue-specific promoters, many of which were known in the art as of the priority date of the instant application, and were known to direct expression in a tissue-specific manner. Specification, paragraphs 0074-0078. Accordingly, the instant specification provides ample guidance for various tissue-specific promoters.

The specification states that a tissue-specific promoter provides for preferential expression in a given tissue. Specification, paragraph 0074. The specification lists a number of epithelial cell-specific promoters, each of which was well known in the art. Specification, paragraph 0078. As of the priority date of the instant application, those skilled in the art were well aware of techniques for determining whether a given promoter controlled expression in a tissue-specific manner. For example, the references listed in paragraph 0078 provide evidence that those skilled in the art could readily determine whether a transgene was being expressed preferentially in intestinal epithelial cells. Accordingly, the specification provides ample guidance as to how to make a transgenic non-human mammal comprising a desaturase-encoding transgene, where the nucleotide sequence encoding the desaturase is operably linked to a tissue-specific promoter.

The Office Action stated that the specification does not teach how to identify a transgenic intestinal SCD mouse and how to use a mouse comprises of an intestinal epithelial promoter operably linked to a nucleic acid sequence encoding SCD, where the mouse expresses rat SCD and exhibits certain phenotypes. However, as noted above, the specification provides ample description of epithelial cell-specific promoters (paragraph 0078); and the references listed in paragraph 0078 provide evidence that those skilled in the art could readily determine whether a transgene was being expressed preferentially in intestinal epithelial cells. The specification provides working examples of how to measure MUFA and PUFA content of tissues. The specification states that where a subject transgenic animal expresses the stearoyl CoA desaturase transgene in epithelial cells of the intestine and/or rumen, food products that have altered MUFA and/or PUFA content include meat. Specification, paragraph 0091. Thus, measuring the MUFA and PUFA content of the muscle of a transgenic animal gives an indication as to whether the SCD is expressed in epithelial tissue. Specification, paragraph 0088. Example 2 describes how to make such a transgenic animal.

Method for producing a non-human transgenic animal

The Office Action stated that the instant specification does not reasonably provide enablement for a method of producing a transgenic non-human animal, comprising introducing any desaturase transgene into a somatic cell, forming a genetically modified somatic cell, transferring the genetically modified nucleus of the somatic cell into a single-celled embryo, generating a genetically modified embryo, and transferring said embryo into a recipient female, where the embryo develops into a transgenic animal in the female.

However, as of the September 17, 2002 priority date of the instant application, those skilled in the art were well aware of how to carry out somatic cell nuclear transfer, to generate a transgenic non-human mammal.

Food products

The Office Action stated that the specification does not reasonably provide enablement for a method for producing a food product comprising harvesting or processing a food product from a transgenic non-human animal, other than milk. Applicants respectfully disagree.

As discussed above, the specification provide ample description of, e.g., transgenic non-human mammals comprising a desaturase transgene operably linked to a tissue-specific promoter, e.g., an epithelial cell-specific promoter, such that the desaturase transgene is expressed in epithelial cells of the intestine and/or rumen, and such that the MUFA and/or PUFA content of the meat of the transgenic non-human mammal is altered. Specification, paragraphs 0078 and 0088. Accordingly, the instant specification is enabling for the full scope of the claims.

Written description

The Office Action stated that the claims contain subject matter which is not described in such a way as to reasonably convey to one skilled in the art that Applicants had possession of the claimed invention as of the filing date. Applicants respectfully traverse the rejection.

Comments regarding the written description requirement of 35 U.S.C.§112, first paragraph

To satisfy the written description requirement of 35 U.S.C.§112, first paragraph, a patent specification must describe the claimed invention in sufficient detail such that **one skilled in the art can reasonably conclude that the inventor(s) had possession of the claimed invention as of the filing date.**

The MPEP §2163 states:

(1) There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed;

(2) The Examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims;

(3) Consequently, rejection of an original claim for lack of written description should be rare;

(4) An Examiner should review the entire application to understand how Applicant provides support for the claimed invention; and

(5) Such a review is conducted *from a standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and the level of skill and knowledge in the art* (emphasis added).

As stated in the MPEP §2163, "In most technologies which are mature, and *wherein the knowledge and level of skill in the art is high*, a written description question **should not be raised** for original claims even if the specification discloses only a method of making the invention and the function of the invention."

MPEP§2163 states that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species; and that a "representative number of species" means that the species which are adequately described are representative of the entire genus. MPEP§2163 states that there may be situations in which one species adequately supports a genus; and that what constitutes a "representative number" is an inverse function of the skill and knowledge in the art.

Those skilled in the art would recognize that, as of the priority date of the instant application, Applicants had possession of the instant invention as claimed.

The Office Action stated that the specification does not teach a representative number of mice comprising different fatty acid desaturases; and stated that, for this reason, any non-human mammal comprising any fatty acid desaturase transgene other than SCD does not meet the written description requirement. Applicants respectfully disagree.

However, as noted above, the specification discloses publicly available sources of nucleotide sequences encoding a variety of fatty acid desaturases, as well as a variety of stearoyl CoA desaturases. Accordingly, those skilled in the art would recognize that Applicants had possession of the invention as claimed. Accordingly, the specification provides adequate written description of fatty acid desaturase transgenes, and transgenic non-human mammals comprising same.

The Office Action stated that the specification does not teach the physical structure, function, and utility of a transgenic non-human mammal comprising a nucleic acid encoding a fatty acid desaturase operably linked to any tissue-specific promoter. However, the instant specification provides working examples for both transgenic mice and transgenic goats, where the desaturase-encoding nucleotide sequence of the transgene is operably linked to a mammary-specific promoter, and where the fatty acid composition of the milk produced by the transgenic animals was altered. Specification, Example 1. The instant specification also provides a detailed description of how to make a transgenic non-human animal, where the desaturase-encoding nucleotide sequence of the transgene is operably linked to an intestinal epithelial cell-specific promoter. Specification, Example 2. In Example 2, the sequence of primers that amplify an intestinal epithelial cell-specific promoter are given. Thus, the specification provides ample description which, together with the knowledge in the art, would lead a person skilled in the art to recognize that Applicants had, as of the priority date of the instant application, possession of the claimed invention.

Claim amendments

Notwithstanding the above remarks, and solely in the interest of expediting prosecution, claim 1 is amended to recite that the transgene comprises a nucleotide sequence encoding a fatty acid desaturase, wherein the fatty acid desaturase-encoding nucleotide sequence is operably linked to a mammary gland-specific promoter, and wherein the transgene is expressed in a mammary gland epithelial cell of said mammal; claim 13 is amended to recite "introducing a transgene comprising a nucleotide sequence encoding a fatty acid desaturase, wherein the fatty acid desaturase-encoding nucleotide sequence is operably linked to a mammary gland-specific promoter"; and claims 20 and 21 are amended to recite that the food product is milk.

Conclusion as to the rejections under 35 U.S.C.§112, first paragraph

Applicants submit that the rejection of claims 1, 3, 5-8, 13-21, and 31-43 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§112, second paragraph

Claims 3, 5, and 39-43 were rejected under 35 U.S.C.§112, second paragraph, as allegedly indefinite.

The Office Action stated that claims 3 and 5 recite the limitation "non-human animal"; and stated that there is insufficient antecedent basis for such.

Claims 3 and 5 are amended to recite "non-human mammal."

The Office Action stated that claims 39-43 recite "mammary gland-specific promoter"; and stated that there is no gland-specific promoter in claim 7.

Claims 39-43 are amended to depend from claim 1, which provides antecedent basis for "mammary gland-specific promoter."

Applicants submit that the rejection of claims 3, 5, and 39-43 under 35 U.S.C. §112, second paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCDV-286.

Respectfully submitted,
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Date: Oct. 6, 2005

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